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| 09/744,146 | 03/29/2001 | Masayuki Machida | 10287.39 | 3956 |

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| EXAMINER | |
|---|---|
| SISSON, BRADLEY L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/744,146 | MACHIDA ET AL. | |
| | Examiner | Art Unit | |
| | Bradley L. Sisson | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *8-11 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 April 2004 has been entered.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 8-11 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude

that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

4. For convenience, claims 35, 36, and 37, the only independent claims, are reproduced below.

35. (Currently Amended) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 10 microns ~~1mm~~, each receptor having a first end and a second end,

wherein the first end of each receptor is bonded with said carrier particle,

wherein said target receptors are single-stranded nucleic acids of predetermined base sequence, wherein the single-stranded nucleic acid is a base sequence of a gene, a base sequence of mRNA, a base sequence of tRNA, a base sequence of rRNA, a base sequence obtained by denaturation of a double stranded nucleic acid or a base sequence obtained by synthesis, and

wherein said target receptors bonded with a single carrier particle have the same or different base sequences;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances;

wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

36. (Currently Amended) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 10 microns ~~1mm~~, wherein said target receptors are double stranded nucleic acids of predetermined base sequence, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a first end of a first single strand bonded with said carrier, and wherein said target receptors bonded with a single carrier particle have the same or different base sequences; wherein the double-stranded nucleic acid is a base sequence of a gene, a base sequence of mRNA, a base sequence of tRNA, a base sequence of rRNA, a base sequence obtained by using the polymerase chain reaction, a base sequence having a recognition sequence of a restriction enzyme at one end, a base sequence generated by annealing, or a base sequence generated by DNA ligase;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of a second single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances;

wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

37. (Currently Amended) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 10 microns ~~1mm~~, wherein said target receptors are double stranded nucleic acids having a predetermined base sequence, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a second end of a first single strand bonded with said carrier, wherein said target receptors bonded with a single carrier particle have the same or different base sequences; wherein the double-stranded nucleic acid is a base sequence of a gene, a base sequence of mRNA, a base sequence of tRNA, a base sequence of rRNA, a base sequence obtained by using the polymerase chain reaction, a base sequence having a recognition sequence of a restriction enzyme at one end, a base sequence generated by annealing, or a base sequence generated by DNA ligase;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the first end of a first single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances;

wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

5. For purposes of examination, the claims have been interpreted as encompassing the use of any nucleic acid that has a length of up to 10 microns, and that said length can be based upon a linear form of a nucleic acid as well as a nucleic acid that has a secondary or tertiary structure so long and the conformation of the nucleic acid presents a length in at least one dimension of up to 10 microns.

6. In accordance with claims 35-37, the nucleic acid has been interpreted as being comprised of a complete "gene," which has been interpreted as encompassing promoter region(s), exons and introns. Said gene has been interpreted as being virtually any and all genes, form any life form and that the 'gene" can be presented in both complete of fragmented form.

Said nucleic acid has also been interpreted as encompassing mRNA, tRNA, rRNA, a sequence obtained by polymerase chain reaction, a nucleic acid that has a restriction site at one end, a sequence that is generated by annealing as well as a nucleic acid generated by action of a DNA ligase.

7. Said labeled complex has also been interpreted as encompassing an infinite number of different nucleic acids.

8. In each instance, the nucleic acid component has been interpreted as having a "predetermined base sequence."

9. The complex of claims 35-37 has also been interpreted as requiring not only prior knowledge of the base sequence of any of the aforementioned nucleic acid embodiments, but that the at least two labeling substances are bound to different fractions of any number of target receptors and that the labeled complex has a "predetermined molar ration of the types of labeled substances."

10. US Patent 6,465,241 B2 (Haronian et al.), column 14, second full paragraph, teach that the length of axial rise per nucleotide in DNA is 3.3 Angstroms or $3.3 \times 10^{-4}$ micrometers. In view of this teaching, applicant's single stranded nucleic acid of a predetermined length would be 30,303 nucleotides long. Accordingly, applicants nucleic acid of a predetermined base sequence, be it a gene, tRNA, rRNA, mRNA, PCR product, comprising a restriction site at one end, is the product of annealing or of synthesis, would have a length up to 30,303 bases.

11. A review of the disclosure fails to find an adequate written description of any one embodiment where a nucleic acid has a length of 30,303 bases, be said nucleic acid tRNA, mRNA, rRNA, a gene, etc.

12. A review of the disclosure fails to find where any Sequence Listing of any nucleic acid has been provided. Yet, as seen in independent claims 35-37, the claims are drawn to a complex that is required to comprise nucleic acids of a predetermined sequence.

13. The failure of the disclosure to set forth any nucleic acids of a predetermined sequence and be labeled with different labels in a "predetermined molar ratio," even when the nucleic acids have the same length and differ by but a single nucleotide does not reasonably suggest that applicant had possession of such a complex. Further, the absence of a description of such mandatory components fails to satisfy the written description requirement of 35 USC 112, first paragraph. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

For the above reasons, and in the absence of convincing g evidence to the contrary, claims 8-11 and 35-37 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

*Response to arguments*

14. At page 9 of the response received 29 April 2004, applicant asserts that they have provided an adequate written description of the claimed complex, asserting that the nature of

nucleic acids was known and described in the specification. Argument is also provided that sequencing was known in the art at the time of the invention. Attention is also directed to US Patent 5,171,534.

15. The above arguments have been fully considered and have not been found persuasive towards the withdrawal of the rejection. As an initial matter, it is noted that each application is considered on its own merits. Accordingly, the aspect of what was or was not issued in another application does not control the prosecution of the instant application.

16. Furthermore, the claims of US Patent 5,171,534 are not drawn to nucleic acid compound, but rather, are drawn to a system for electrophoretic analysis of oligonucleotide fragments. Unlike the claims of the '534 patent, the instantly claimed complex is required to comprise nucleic acids of a predetermined sequence, have a predetermined molar ratio. The specification provides no description of any nucleic acids that have a predetermined nucleotide sequence and which also exist in a predetermined molar ratio on a carrier molecule, and that such an arrangement that there is no "major influence by energy movement or quenching among the labeled substances."

17. To the extent that the specification is asserted t provide an adequate written description of the molecules, it is noted that the description provided is generic in that it describes the nucleic acids as being DNA, mRNA, rRNA, tRNA, the product of an amplification reaction, etc. Such descriptions are not considered to constitute an adequate written description of any nucleic acid of a "predetermined sequence," much less provide an adequate written description of virtually an infinite number of nucleic acids of both predetermined nucleotide sequence, predetermined

molar ratio, and being such that there is no "major influence by energy movement or quenching among the labeled substances."

18. While the claims recite how they re to function, the specification does not teach what nucleotide sequences can be brought together. In short, the specification has not provided an adequate description of the structure of nucleic acids that permit the required function.

19. Therefore, and in the absence of convincing evidence to the contrary, claims 8-11 and 35-37 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

20. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

21. Claims 8-11 and 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

22. The term "major" in claims 35-37 is a relative term that renders the claims indefinite. The term "major" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 8-11, which depend from said claims 35-37, fail to overcome this issue and are similarly rejected.

23. Claims 35-37 are indefinite a to how one obtains a predetermined base sequence when simply denaturing double stranded nucleic acids. Seemingly one can denature virtually any

nucleic acid, or mixture of nucleic acids by heating the mixture, yet such separation would not necessarily result in the identification as to how any predetermined sequence, or predetermined molar ratio of nucleic aids is achieved. Claims 8-11, which depend from claims 35-37, fail to overcome this issue and are similarly rejected.

### *Claim Rejections - 35 USC § 102/103*

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

25. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claims 8-11 and 35-37 are rejected under 35 U.S.C. 102(a and e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,124,092 (O'Neil et al.).

30. O'Neil et al., disclose the immobilization of "recovery primers" and "recovery tags" (nucleic acid probes and nucleic acid primers; applicants' "target receptors" and "single-stranded nucleic acids of a predetermined base sequence').

31. O'Neil et al., column 16, provides a listing of various solid supports (applicants' carrier particle) to which one or more nucleic acids are bound.

32. O'Neil, column 11, teaches that the nucleic acids can be labeled with any of a variety of labels, including fluorescent labels, chemiluminescent labels, etc.

33. O'Neil et al., column 6, teaches that in one embodiment the nucleic acid can be of from 18-36 nucleotides long (primers). O'Neil et al., also discloses performing primer extension reactions, where a fluorescently labeled chain terminator is incorporated into the primer extension product. The aspect of creating a single stranded nucleic acid that is bound to a solid support (carrier) at one end and has a label a the other end (chain terminated sequencing reaction product) is considered to meet the limitation that the immobilized nucleic acids can be of considerably longer length, e.g., tens of thousands of nucleotides long.

34. O'Neil t al., are considered to meet the limitation that the nucleic aids are present in a predetermined molar ratio as they are disclosed as being used in PCR and sequencing assays, which require the usage of known concentrations of reactants.

35. In the event that O'Neil et al., do not anticipate the claimed invention, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a compound comprising nucleic acids immobilized to a carrier where the nucleic acids are of a predetermined sequence, are labeled at the end opposite to that bound to the carrier, and are present in a predetermined molar ratio as such is disclosed as being useful in conducting hybridization assays, amplification assays, and sequencing assays.

36. For the above reasons, and in the absence of convincing evidence to the contrary, claims 8-11 and 35-37 are rejected under 35 U.S.C. 102(a and e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,124,092 (O'Neil et al.).

***Conclusion***

37. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

38. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

39. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
12 May 2004